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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/706,765	11/12/2003	Richard Lipsky	LIPSKY 3.0-001	7803

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EXAMINER	
KIM, JENNIFER M	
ART UNIT	PAPER NUMBER
1617	
MAIL DATE	DELIVERY MODE
03/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/706,765	LIPSKY, RICHARD	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5,13-20 and 22-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,5,13-20 and 22-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed December 10, 2007 have been received and entered into the application.

Applicants' arguments with respect to claims 1, 4, 5, 13-20 and 22-31 have been considered but are moot in view of the new ground(s) of rejection.

It is noted that claims 1, 4, 5, 13-20 and 22-31 have been examined only to the extent of Applicant's elected species, naloxone, as an opioids antagonist.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Fink (1972).

Fink teaches naloxone (n-allynoroxymorphone) is eight times as effective as nalorphine in antagonizing opiate effects in animals. Fink teaches the effects of naloxone given in acute **single** intravenous doses, and in chronic oral doses. Fink teaches that using heroin challenges as his index, Fink observed complete blockade of

heroin by intravenous administration of 1.0 mg of naloxone. (page 174, right-hand side, first full paragraph). Fink teaches that by increasing the daily **single oral dosages to 3.0gm**, he achieved blockade to heroin for 24 hours. (It is noted that Fink's single 3.0grm oral dosage is greater than 0.6mg/kg; subject weighing 50kg based on the specification [0030]). (see Applicants' claim 31).

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over McDonald et al. (April 2001) of record in view of Fink (1972).

McDonald et al. teach that opioids detoxification was produced by infusion of 25mg naloxone for 30 minutes, Followed by a 24 hour infusion of 1 mg per hour. (abstract). Therefore, McDonald et al's a daily (24 hour period) naloxone is 50mg.

McDonald et al. do not teach the administration of 50mg naloxone in a single dosage.

Fink teaches that naloxone can be given in acute single intravenous doses. (page 174, right-hand side, first full paragraph).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to administer naloxone in divide daily dosages of 50mg taught by McDonald et al. in a single dosage for the treatment of opiate addiction or detoxification because Fink teaches that the naloxone can be administered in acute single

intravenous doses. One would have been motivated to make such a modification in order to successfully treat opiate detoxification in a single convenient intravenous dose of naloxone in view of Fink. There is a reasonable expectation of successfully treating opiate detoxification with 50mg single dosage of naloxone because the effectiveness of 50mg daily dosage administration of naloxone in treatment of opioids detoxification is well taught by McDonald et al. and the effects of naloxone given in acute single intravenous disease is well taught by Fink.

Claims 4, 13-20 and 22-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over McDonald et al. (April 2001) in view of Legarda Ibanez (U.S.Patent No. 6,103,734) and further in view of Takrouri et al. (2002), Gooberman et al. (U.S.Patent No. 5,789,411), all of record.

McDonald et al. teach that opioids detoxification was produced by infusion of 25mg naloxone for 30 minutes, followed by a 24 hour infusion of 1 mg per hour. (abstract). Therefore, McDonald et al's a daily (24 hour period) naloxone is 50mg. Accordingly, McDonald et al's daily dosage of naloxone in mg/kg is 1mg/kg. This is within Applicants' ranges set forth in claims 13 and 22).

McDonald does not teach the administration of dextromedetomidine (PRECEDEX) and the rate of administration and detoxification process comprising anesthetizing, intubating, stabilizing the patient, giving Valium, Xanax, Trazodone, antiemetics and antiperistaltic agents, administration of antihistamine agent prior to administering opioids antagonist and further administering nalmefene (REVEX).

Legarda Ibanez teaches a method to suppress opiates dependence with combination of chemical compounds used as a medicament comprising administering antiemetic, sedating or anesthetizing agent, H2-antihistamine, benzodiazepine and alpha-adrenergic agent such as clonidine. (claims 1-13). Legarda Ibanez teaches that an alpha-adrenergic agonist such as clonidine increases sedation and diminishes the symptomatology of the syndrome of opiate abstinence. (column 2, lines 39-42). Legarda Ibanez teaches the combination of chemical compounds in opiate dependence treatment allows an ultra rapid approach for the detoxification of polydrug users who are addicted to heroin and/or Methadone or other opiates. (column 3, lines 12-15).

Takrouri et al. teach that dexmedetomidine (Precedex) is a potent new alpha-2 adrenoreceptor agonist more than 7 times of alpha –2 activity than clonidine. Takrouri et al. teach that dexmedetomidine has potent sedative, analgesic and sympatholytic effects blunt the cardiovascular responses without unexpected toxicity. (abstract).

Gooberman et al. teach that rapid opioids detoxification procedure with naloxone comprising sedating a patient with an anesthetic agent comprising administering a diarrhea suppressant agent, neuromuscular blocking agent. (abstract, claims). Gooberman et al. also teaches that nalmefene (Revex) can be administered to the patient after the initiation of the withdraw with naloxone. (column 5, lines 34-37).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the opioids detoxification method taught by McDonald and employ combination of chemical compounds such as antiemetic, sedating or anesthetizing agent, H2-antihistamine, benzodiazepine and alpha-adrenergic agent

taught by Legarda Ibanez because Legarda Ibanez teaches that the combination of chemical compound with naloxone detoxification allows an ultra rapid approach for the detoxification of polydrug users who are addicted to heroin and/or Methadone or other opiates. With regard to the employment of Precedex (dexmedetomidine) and nalmefene (Revex) as well as the specific benzodiazepine (e.g. Valium, Xanax) are all deemed obvious because the usefulness of the active agents in combination with naloxone in opioids detoxification has been collectively taught by the combined teachings of the references. It would have been obvious to one of ordinary skill in the art to further modify the method of Legarda Ibanez and replace clonidine with dexmedetomide as an alpha adrenergic agonist in view of Takrouri et al. who teach that dexmedetomidine is more potent than clonidine in treating sedation without toxicity. It would have been obvious to one of ordinary skill in the art to further incorporate Revex in opioids detoxification comprising naloxone as modified by Legarda Ibanez because the administration of nalmefene (Revex) to a patient after the initiation of the withdraw process with naloxone is well known in view of Gooberman et al. The amounts of active agents to be used, the pharmaceutical forms, e.g., tablets, etc; mode of administration, flavors, surfactant are all deemed obvious since they are all within the knowledge of the skilled pharmacologist and represent conventional formulations and modes of administration. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

None of the claims are allowed.

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jennifer Kim/
Primary Examiner, Art Unit 1617

Jmk
March 17, 2008